Cystic Fibrosis and Sleep

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KEYWORDS

• Sleep-disordered breathing • Hypoxemia • Respiratory insufficiency • Hypoventilation
• Noninvasive ventilation

KEY POINTS

- Patients with cystic fibrosis experience both sleep disruption and gas-exchange abnormalities during sleep.
- Symptomatically, cough and pain are reported in advanced stages of the disease in most individuals.
- Noninvasive ventilation and supplemental oxygen is frequently helpful in mitigating the adverse effects of nocturnal hypercapnia and hypoxemia.

INTRODUCTION

Cystic fibrosis (CF) pulmonary disease is characterized by chronic bacterial infection, gradual airway obstruction, and bronchiectasis, resulting in hypoxemia, hypercapnia, and increased work of breathing. In addition, CF has several features that adversely affect sleep including chronic cough, musculoskeletal pain, frequent defecation, gastrointestinal reflux, abdominal discomfort, and sometimes overnight enteral feeding. Medication usage and comorbid mood disorders may also contribute to the poor quality of sleep observed in CF. Many studies have reported considerable subjective sleep complaints with only modest objective polysomnographic changes. In general, sleep disruption or restriction has been associated with cardiovascular, metabolic, immune, and neurocognitive dysfunction. These abnormalities may exacerbate the CF-related insulin-dependent diabetes, pulmonary hypertension, frequent sinopulmonary infections, and mood disturbances. Poor sleep quality and excessive daytime sleepiness are commonly reported by CF patients and their caregivers, and correlate adversely with quality-of-life measures. In principle, treatment of gas-exchange abnormalities and sleep fragmentation could improve the quality of life and mitigate long-term complications of CF. This review focuses on the bidirectional interaction between sleep and CF.

SUBJECTIVE SLEEP DISTURBANCES

Most studies of subjective sleep quality in CF report disturbed sleep in more than 50% of patients, especially those with advanced lung disease.[1–3] Common sleep complaints include sleep-onset insomnia,[4] frequent awakenings, night cough, snoring, excessive daytime sleepiness, headaches, pain, frequent defecation,[4] anxiety, and reflux. Even when clinically stable, CF patients report more frequent awakenings with cough.[5] Longitudinal studies show that moderate to severe sleep complaints often persist over a period of years in 10% of CF patients.[6] In addition, CF patients are less likely to seek medical attention for their sleep problems than for their other concerns, and pulmonologists are most commonly consulted for their sleep complaints.[6] Sleep quality improves significantly following a hospitalization or rehabilitation admission (including intensive chest physical therapy, antibiotics, and nutritional counseling).

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Sleep complaints have been identified in both pediatric and adult CF patients. A population-based study of CF children between 0.5 and 5 years revealed that small and moderate to large sleep problems were present in 32% and 22%, respectively.[7] Parents also report that their children with CF have more morning sleepiness.[4] In older children and adolescents with CF (mean age 14.2 years), 44% complain of sleep-onset insomnia and 39% of sleep-maintenance insomnia, and 74% report excessive daytime sleepiness.[8] In a population-based study of adults with CF, excessive daytime sleepiness (EDS) as assessed with the Epworth Sleepiness Score was more common in CF patients than in control subjects (20% vs 7%).[9] Using the Pittsburgh Sleep Quality Index, adults with CF had poorer sleep quality in comparison with controls, which correlated with adverse quality-of-life measures.[9] Disturbed sleep quality is particularly common in CF patients awaiting transplant,[10] although there is a poor association with gas-exchange abnormalities.[1]

Pulmonary CF exacerbations in school-aged children[11] and adults[12] are usually accompanied by sleep disruption attributed primarily to coughing. Many patients report sleeping during the day as a consequence of inability to sleep at night.[11,12] Conversely, when describing improvement in their condition following the initiation of therapy, improvements in sleep were an important determinant of perceived exacerbation resolution.[11–13] Moreover, treatment of a CF pulmonary exacerbation results in decreases in sleepiness[14] and nocturnal cough.[15] However, one study reported that frequency of nocturnal cough did not significantly change following 14 days of antibiotics, despite clinical and spirometric improvement.[16]

Healthy individuals cough less than 1 time per hour, and rarely during sleep.[17] In patients with respiratory disorders, nocturnal coughing is typically observed during periods of wakefulness lasting at least 1 minute, rather than being associated with a brief arousal.[18] Nocturnal coughing was documented in more than 80% of children with CF, compared with a historical prevalence of 5% of healthy children.[16,17] Stable children with CF (mean age 12.8 years, forced expiratory volume in 1 second [FEV_1] 72%) were reported to cough 0.6 to 0.9 seconds per hour overnight, and this was more prevalent in those with more advanced lung disease.[19] Thus, although stable children with CF cough more than healthy children, the duration of this coughing is relatively brief. In a large questionnaire study (N = 99), 63% of CF patients reported that cough always or sometimes disrupted sleep,[20] and the severity was worse with decreasing FEV_1.[21]

The relationship between objective and subjective cough measures in children is modest.[15,22] Objective cough-recording devices have documented nocturnal cough in CF patients during a pulmonary exacerbation, often in the absence of patient-reported coughing.[16] CF patients cough at least 3 times more frequently during wakefulness in comparison with sleep.[16] Another group of clinically stable CF patients (mean age 26 years, FEV_1 65%) reported 41 coughs per hour awake and 2 per hour asleep, with no correlation between objective and subjective cough rates.[21] The presence of cough resulting in fragmented sleep can impede the progression to rapid eye movement (REM) sleep.[23]

Between 40% and 60% of CF patients will complain of pain, frequently severe, which is associated with poor sleep quality.[5] In a retrospective study of chronic pain in CF patients older than 5 years who died, chronic pain was seen in 84% of patients including headaches (55%), chest pain (65%), back pain (19%), and abdominal pain (16%).[24] Of importance is that hypercarbia or hypoxia was reported to be the primary cause of headache, suggesting a potentially treatable condition. Opiate medications were used in more than 50% of patients, but no respiratory complications were reported.[24] Finally, a case of restless legs syndrome in a 22-year-old CF patient was reported with chronic hemoptysis and nonrestorative sleep, which resolved following iron supplementation.[25]

OBJECTIVE SLEEP QUALITY

Although subjectively poor sleep quality is common in CF patients, especially with advanced disease, most adult studies demonstrate only small objective abnormalities including lower sleep efficiency,[8,26] less REM sleep,[8,26] and an increased arousal index.[2,8,27] Children with CF also are reported to have lower sleep efficiency, reduced REM sleep, and increased electrocortical arousals compared with control children.[28] By contrast, infants with CF had a sleep architecture similar to that of healthy controls.[29] In addition, there are many polysomnographic studies in CF patients that have shown no or minimal differences in sleep architecture.[2,30,31] However, numerous studies document poor-quality sleep in the setting of CF pulmonary exacerbation.[14] Pulmonary exacerbations are associated with more wakefulness after sleep onset, less REM sleep, and more hypoxemia, which all improved significantly following approximately 2 weeks of inpatient therapy.[14] Most episodes of hypoxemia are not associated with arousal.[32]